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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,487	12/12/2003	Ulrich Bothe	2843	1882

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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,487	BOTHE ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio, Ph.D.	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/17/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

First Office Action on the Merits

Priority

1. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim

filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1 and 4-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims recite a "use" without setting forth any steps involved in the process and, thus, results in an improper definition of a process, i.e., results in a claim that is not a proper process claim under 35 USC § 101 (see MPEP § 2173.05(q)).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 5 and 6 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The court has held that an adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119, F.3d

1559, 1568 (Fed. Cir. 1997). The Federal Circuit has also adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 USC 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, "including, inter alia, "functional characteristics when coupled with a known or disclosed correlation between function and structure...". *Enzo Biochem, Inc. v. Gen-Probe.*, 296 F.3d, 316, 1324-25 (Fed. Cir. 2002).

The present specification lacks an adequate description of the claimed subject matter because there is insufficient descriptive support for the compounds, apart from compounds of formula I as defined by the present specification, utilized in the claimed invention, i.e., glucocorticoid receptor antagonists having the binding affinity as defined by the instant claims. There is a lack of correlation between said functional characteristic and structure(s) apart for those encompassed by formula I and, thus, the skilled artisan would be unable to envision the full scope of compounds necessary for practice of the claimed invention. Thus, the claims fail to comply with the written description requirement.

6. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the utilization of the claimed compounds for therapy of the claimed disorders/diseases, does not reasonably provide enablement for

utilization for the prophylaxis of said disorders/diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

The claimed invention is directed to compositions for the prophylaxis and therapy of glucocorticoid receptor antagonists. Webster's dictionary defines "prophylaxis" to be inclusive of "prevention". However, the present specification lacks guidance or working example(s) of how the skilled artisan in the relevant art would utilize the claimed composition for the "prevention" of the recited disorders and/or how the skilled artisan would determine a person in need of said preventative measures. Because of the lack of guidance and/or working example(s), the quantity of experimentation necessary to practice the claimed invention commensurate with the instant claims would be undue.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because they merely recite a "use" without any active, positive steps delimiting how this use is actually practiced and, thus, it is unclear what process is encompassed by the claimed invention (see MPEP § 2173.05(q)).

For the purpose of art rejection, the claims are interpreted as being drawn to a composition.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Gebhard et al. (US 5,620,966).

Gebhard et al. teaches 11,21-bisphenyl-19-norpregnane derivatives, such as (11β,17α)-11-[4-(dimethylamino)phenyl]-17-hydroxy-21-[4-(methylsulfonyl)phenyl]-19-norpregna-4,9-dien-20-yn-3-one (see the entire article, especially col. 1, line 32 – col. 2,

line 12; Tables I and II; Example 1 and 4-9). The reference teaches (a) the compounds have selective affinity for glucocorticoid receptors and anti-glucocorticoid activity in vivo (see for example, col. 1, lines 32-62); (b) the compounds are useful in treating glucocorticoid-dependent diseases (see for example, Abstract); (c) various routes of administration (see col. 3, lines 24-40) and (d) a preferred dosage of 0.001-100mg per kg (see col. 3, lines 24-27). The compositions taught by the reference are encompassed by the instant claims.

11. Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Groen et al. (US 6,072,068).

Groen et al. teaches 16-hydroxy-11-(substituted phenyl)-estra-4,9-diene derivatives such as (11β,16α,17β)-11-(4-methylphenyl)16,17-dihydroxy-17-(1-propynyl)estra-4,9-dien-3-one (see the entire article, especially col. 1, line 28 – col. 2, line 65). The reference teaches (a) the compounds have a high selective affinity for glucocorticoid receptors and potent in vivo anti-glucocorticoid activity (see for example, col. 1, lines 22-25); (b) the compounds are useful in treating glucocorticoid dependent diseases (see for example, col. 3, lines 31-37); (c) various routes of administration (see col. 4, lines 1-35) and (d) dosages of 0.001-50 mg per kg (col. 3, lines 50-57). The compositions taught by the reference are encompassed by the instant claims.

12. Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Peeters (WO 95/04536).

Peeters teaches antiglucocorticoid steroids such as (11β,17α)-11-[4-(dimethylamino) phenyl]-17-hydroxy-21-[4-methylsulfonyl)phenyl]-19-norpregna-4,9-dien-20-yn-3-one for use in the treatment of anxiety (see the entire article, especially Abstract; page 1, lines 5-7; page 2, line 17 – page 3, line 29; page 4, lines 1-12). The reference teaches (a) the preferred R_2 group is phenyl which is substituted in the para position with the -N(X)(Y) group or in the meta position with OCH_3 or SCH_3 (see page 4, lines 19-25); (b) various routes of administration and preferred daily dosage of 0.001 to 10 mg/kg (see page 7, lines 1-20). The compositions taught by the reference are encompassed by the instant claims.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gebhard et al. (US 5,620,966) and Philibert et al. (US 4,477,445) in combination.

Gebhard et al. teaches 11,21-bisphenyl-19-norpregnane derivatives, such as (11β,17α)-11-[4-(dimethylamino)phenyl]-17-hydroxy-21-[4-(methylsulfonyl)phenyl]-19-norpregna-4,9-dien-20-yn-3-one (see the entire article, especially col. 1, line 32 – col. 2, line 12; Tables I and II; Example 1 and 4-9). The reference teaches (a) the compounds

have selective affinity for glucocorticoid receptors and anti-glucocorticoid activity in vivo (see for example, col. 1, lines 32-62); (b) the compounds are useful in treating glucocorticoid-dependent diseases (see for example, Abstract); (c) various routes of administration (see col. 3, lines 24-40) and (d) a preferred dosage of 0.001-100mg per kg (see col. 3, lines 24-27).

The instant claims differ from the reference by reciting compounds that are positional isomers of the prior art compounds. For example, the genus taught by the reference includes compounds having a 4-alkoxy substituted phenyl in the 11β-position. However, a compound that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. *In re Norris*, 179 F.2d 970, 84 USPQ 458 (CCPA 1970). In addition, Philibert et al. teaches an equivalent between antiglucocorticoid compounds having a 4- or 3-substituted phenyl ring in the 11β-position . Therefore, it would have been obvious to the skilled artisan in the art at the time of the present invention to make the compounds of Gebhard having a 3-substituted phenyl ring in the 11β-position as taught by Philibert et al. with the reasonable expectation that the compounds made would be useful antiglucocorticoid compounds.

15. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peeters (WO 95/04536).

Peeters teaches antiglucocorticoid steroids such as (11β,17α)-11-[4-(dimethylamino) phenyl]-17-hydroxy-21-[4-methylsulfonyl)phenyl]-19-norpregna-4,9-

dien-20-yn-3-one for use in the treatment of anxiety (see the entire article, especially Abstract; page 1, lines 5-7; page 2, line 17 – page 3, line 29; page 4, lines 1-12). The reference teaches (a) the preferred R_2 group is phenyl which is substituted in the para position with the -N(X)(Y) group or in the meta position with OCH_3 or SCH_3 (see page 4, lines 19-25); (b) various routes of administration and preferred daily dosage of 0.001 to 10 mg/kg (see page 7, lines 1-20).

The instant claims differ from the reference by reciting compounds not exemplified by the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including that of the instant claims, because an ordinary artisan would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as the genus as a whole. For example, based on the cited prior art, it would have been obvious to the skilled artisan in the art to modify the prior art compound, (11β,17α)-11-[4-(dimethylamino) phenyl]-17-hydroxy-21-[4-methylsulfonyl)phenyl]-19-norpregna-4,9-dien-20-yn-3-one, making (11β,17α)-11-[3-(methoxyphenyl]-17-hydroxy-21-[4-methylsulfonyl)phenyl]-19-norpregna-4,9-dien-20-yn-3-one as recited by the instant claims (see for example, claim 3, compound #3) with the reasonable expectation that the compound obtained would be useful in treating anxiety as taught by reference.

Other Matters

16. The data presented in the present specification is noted. However, the comparison is not persuasive because it is not with the closest prior art compound. It is noted that the tested prior art compound in addition to being substituted in the 4- instead of the 3-position also has different R1 and R2 groups.

Telephone Inquiry

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1617

BB
August 14, 2006